Claim 3 is objected to under 37 CFR 1.75 as being a substantial duplicate thereof of claim 1, however since claims 1-4 have been deleted the objection is moot. Though Examiner had not objected to claims 7 and 5 since the same issue exists in these claims, Applicants traverse the 37 CFR 1.75 objection with respect to claims 7 and 5 here to avoid any future objections.

With respect to the objection under 37 CFR 1.75 against claim 7 (as well as claim 3), there are three types of diseases defined within "arteriosclerosis". First, "atherosclerosis", which is the disease that attacks the large arteries and is also called "pultaceuous arteriosclerosis", second, "medial sclerosis", which is the disease that attacks medium sized arteries, and third, "arteriocapillary sclerosis", which attacks thin blood vessels and is also called "arteriolar sclerosis" or "arteriosclerosis". The term "atherosclerosis" set forth in claim 7 is a subordinate concept of the term "arteriosclerosis" set forth in claim 5 and claim 7 is not a substantial duplicate of claim 5.

Therefore Applicants respectfully request that the 37 CFR 1.75 objection with respect to claim 7 be withdrawn.

Claims 5-10 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for treating arteriosclerosis or slowing its progression, does not reasonably provide enablement for preventing or curing arteriosclerosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants have amended claim 5 to include "A method of treating" and deleted the "preventing and curing" language from the claim. The amendment to claim 5 should obviate the 35 U.S.C. §112, first paragraph rejection with respect to claims 5-10 and Applicants respectfully request that the 35 U.S.C. §112, first paragraph rejection be withdrawn.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Each of claims 1 and 5 lacks positive

antecedent basis for the "hydrogen atom of the hydroxyl group in the saccharide residue" because each saccharide residue has more than one hydroxyl group. Thus the claims are indefinite.

Applicants have deleted claims 1-4 therefore the issue with respect to claim 1 is moot. With respect to claim 5, Applicants have amended claim 5 to include language that optionally a lower alkyl group or a lower acyl group can be substituted for the hydrogen atom at all or independently of each other at any of the hydroxyl groups of the saccharide residue.

Next, claim 8 is rejected under 35 U.S.C. §112, second paragraph, as lacking antecedent basis for the "method" of claim 1 because claim 1 recites an "agent." Applicants have amended claim 8 to depend from claim 5, which has antecedent basis for the "method" of claim 8, thus obviating the rejection under 35 U.S.C §112, second paragraph.

Based on the amendments to both claims 5 and 8 above, Applicants respectfully request that the 35 U.S.C. §112, second paragraph rejection be withdrawn.

Claims 1-4 are rejected under 35 U.S.C. §102(b) as being anticipated by MURASE et al. (A1). Applicants have deleted claims 1-4 thus obviating the 35 U.S.C §102(b) rejection and Applicants respectfully request that the rejection be withdrawn.

Claims 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over MURASE et al. (A1) in view of CYNSHI et al. (B3). Examiner states that Applicant claims a method for "preventing and curing arteriosclerosis" by administering a chromal glucoside. This rejection is made based on the assumption that "preventing and curing arteriosclerosis" might possibly have been intented to encompass treating arteriosclerosis or slowing its progression.

Examiner states that MURASE teaches that formation of lipid peroxides are known to have a bearing on diseases including arteriosclerosis (see column 1, lines 14-23), and that the chromanol glucosides taught therein are antioxidants (see Examples 9 and 10 and the corresponding Figures). However, Examiner states that MURASE does

not specifically state that the chromanol glucosides taught therein can be used to treat arteriosclerosis. Also, Examiner states that since CYNSHI teaches that antioxidants are known in the art to be useful as antiatherogenic agents it would have been obvious for a person of ordinary skill in the art at the time of the invention to use a chromal glucoside, which have antioxidant properties, as taught by MURASE for treating arteriosclerosis or slowing its progression.

Applicants respectfully traverse. It is common knowledge in the medical field that oxygen radicals take part in the promotion and advancement of various diseases. Attempts to apply antioxidants to the prevention and cure of diseases in which the oxygen radicals take part have been published in the attached journal [refer to page 184, right column, lines 8-5, and table 1 on page 185, "Chemistry and Organisms", Vol. 30, No. 3, 1992].

In the case of applying an anti-oxidant substance (radical sequestration type anti-oxidant) to an organism, however, the anti-oxidant activity of this substance is greatly swayed by numerous factors such as the chemical reactivity of the anti-oxidant substance itself to a radical, the reactive site of the anti-oxidant, the local concentration and the ease of mobility of the anti-oxidant, the behavior of the radical originating in the anti-oxidant substance, the interaction with other anti-oxidants, the absorption in an organism, the distribution, the retention, the metabolism, the toxicity and the safety as described on page 107, right column, lines 9-15 of "Journal of Japan Petrochemical Society," Vol. 46, No. 10, 1997. The free radical, as aptly called the "double edged sword" not only functions as a promoter of a morbid state but also proves highly important as a system for protecting an organism. Anti-oxidants do not exclusively eliminate free radicals. This fact results in the major cause for rendering the clinical application of the anti-free radical therapy difficult. Because a given substance possesses an anti-oxidant activity, it does not necessarily follow that this substance can be applied to a disease in which the active oxygen radical takes part. In the case of a given anti-oxidant substance which is useful for curing a specific disease caused by oxygen radicals, the adaptability of this substance toward curing other diseases caused by oxygen radicals is highly unpredictable even by those skilled in the art.

On the other hand, many factors are believed to be associated with the crisis and formation of arteriosclerosis and free radicals and oxygen radicals are only part of these factors. As stated in the present specification, though the use of an anti-oxidant has been tried in treating arteriosclerosis and *in vitro* tests have been performed on numerous antioxidants which have demonstrated that these agents have been effective in inhibiting the oxidation of LDL (lines 16-20, page 2 of the specification), no animal test has produced a report to the effect that the sole administration of a water-soluble antioxidant has inhibited arteriosclerosis. It is, therefore, inferred that the conventional water-soluble antioxidant is incapable of reacting at the site fit for preventing the oxidation of LDL *in vivo* from the affects of oxygen radicals (lines 17-22., page 3 ibid.).

A review of the history of the development of pharmaceutical preparations clearly denies such simple inference that a substance can be utilized as an agent for treating arteriosclerosis because it possesses anti-oxidant properties. Whether or not a given compound is effective as an agent for treating arteriosclerosis is a question not definitively answered unless it is actually given a deliberate pharmacological test. The truth of this assertion is self-evident from the fact that no anti-oxidant agent has yet been authorized as a pharmaceutical preparation for treating arteriosclerosis though the relationship between oxygen radicals and arteriosclerosis was reported some ten years ago.

The references only suggest that anti-oxidants can be useful for treating arteriosclerosis, and MURASE only describes the *in vitro* anti-oxidant activity of the chromanol glycoside. Notwithstanding a substance found to be active *in vitro* as an anti-oxidant, the description of this fact does not necessarily afford a way of predicting the behavior to be manifested by the substance *in vivo*. Though Applicants are aware that under 35 U.S.C. §101, for lack of utility, *in vitro* testing is all that is needed, however there is a lack of *in vitro* testing that directly correlates a compounds inhibitory properties toward treating arteriosclerosis. More still, the question of whether or not the substance is effective particularly in dealing with the arteriosclerosis among numerous other diseases in which the oxygen radical is suggested to take part (see mentioned "Chemistry and Organisms") cannot be solved without performing clinical applications.

Furthermore, the instant invention, as is clear from the description of the specification, is based on the *in vivo* pharmacological action of the chromanol glycoside in varying models. Specifically, the present inventors, as a result of their diligence, pursued in studying the relationship between arteriosclerosis and anti-oxidants and found among a host of existing anti-oxidant substances, the compounds of the present invention as being effective in dealing with the specific disease of arteriosclerosis. Therefore, it would not be such that one skilled in the art could have conceived it based on the references.

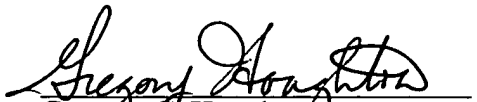
Despite the references cited and based on the above arguments directed toward the 35 U.S.C. §103(a) rejection, the Examiner has not provided any evidence that suggests that it would have been obvious to one skilled in the art at the time the invention was made to have the specifically claimed compounds. Absent such a showing of evidence, the Examiner has impermissibly used "hindsight" by using the Applicant's teaching as a blueprint to hunt through the prior art for the claimed elements and combine them as claimed. *In re Zurko*, 111 F.3d 887, 42 USPQ2d 1476 (Fed. Cir. 1997); *In re Vaeck*, 947 F.2d 488, 20 USPQ2D 1438 (Fed. Cir. 1991). Such an approach would be "an illogical and inappropriate process by which to determine patentability." *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996).

Based on the foregoing, Applicants respectfully request that the rejection of claims 5-10 under 35 U.S.C. 103(a) as being unpatentable over MURASE et al. (A1) in view of CYNSHI et al. (B3) be withdrawn.

The application is now believed to be in a condition for allowance and an early notification thereof is respectfully requested. The Examiner is invited to contact the undersigned should she believe this would expedite prosecution of this application. It is believed no fee is required.

The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,



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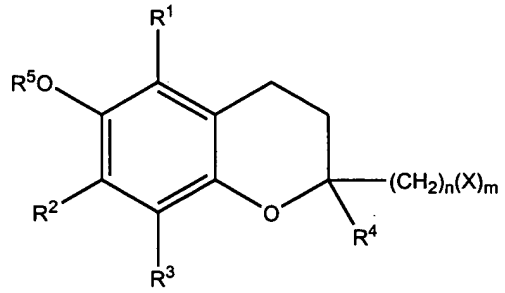
Marked-Up Version of Rewritten Claims.

The subject matter to be added is in bold and underlined and the subject matter to be deleted is in bold and has been bracketed with square brackets.

In the Claims:

5. (Amended) A method for **treating** **[preventing and curing arterosclerosis]** **arteriosclerosis**, the method comprising administering to a subject an agent having as an active component thereof a chromanol glucoside represented by the following general formula (1)



(1)

[(]wherein R^1, R^2, R^3, and R^4 are the same or different and are each a hydrogen atom or a lower alkyl group, R^5 is a hydrogen atom, a lower alkyl group, or a lower acyl group, X is a monosaccharide residue or an oligosaccharide residue optionally having a lower alkyl group or a lower acyl group **substituted** **[substitute]** for the hydrogen atom **[of]** **at all or independent of each other at any of** the hydroxyl **groups** **[group]** in the saccharide residue, n is an integer in the range of 0-6, and m is an integer in the range of 1-6**[)]**.

8. (Amended) The method of claim **5** **[1]** wherein said agent is in aqueous preparation.